REMARKS

Claim 27 has been canceled without prejudice or disclaimer. Claims 39-58 are withdrawn pursuant to the restriction requirement. Claims 28 and 38 have been amended. Subsequent to the entry of the present amendment, claims 2-25, 28-33 and 38 are pending and at issue. These amendments add no new matter as the claim language is fully supported by the specification and original claims.

I. Election/Restriction

The Office Action alleges that newly submitted claims 39-58 are directed to an invention that is independent of distinct from the invention originally claimed.

Applicants withdraw claims 39-58.

II. Claim Objections

Claims 2-25, 27-33 and 38 are objected to. The Office Action alleges that Claims 2-25, 27-33 may not depend from a claim that occurs after the dependent claim 38 and must depend from a claim that is chronologically before the dependent claims.

Applicants respectfully disagree with this objection. A review of MPEP 608.01(j) and 37 CFR 1.126, both titled "NUMBER OF CLAIMS" does not have such a requirement. Both sections indicate that once claims are ready for allowance, the examiner will renumber the claims consecutively in order. Applicants will wait until that time to renumber. Accordingly, reconsideration and withdrawal of the objection is respectfully requested

III. Rejections under 35 U.S.C. §112, First Paragraph

Claims 2-25, 27-33 and 38 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not described in the specification in such a way as to enable

one of skill in the art to make or use the invention. Specifically, the Office Action alleges that the specification fails to provide sufficient support for "a plurality of fractions" in claim 38. Applicants traverse this rejection as it may apply to the amended claims

Applicants have amended claim 38 to remove the term "a plurality of fractions", rendering this rejection moot.

IV. Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 2-25, 27-33 and 38 are rejected under 35 U.S.C. § 112, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Office Action alleges the claim 38 phrase "each fraction containing an individual protein or protein fragment" is vague. Applicants traverse this rejection as it may apply to the amended claims.

Applicants have amended claim 38 to remove the term "each fraction containing an individual protein or protein fragment", rendering this rejection moot.

V. Rejections under 35 U.S.C. § 103

A. Claims 2-5, 10, 14-17, 20-26, 29-33 and 38 are rejected under 35 U.S.C. §103(a) as allegedly obvious over Natan et al. (US 6,242,264) in view of Natan et al. (US 6,579,721). This rejection is respectfully traversed.

The Office action alleges that "Natan et al. ('264) teaches a method comprising: chromatographically separating proteins and protein fragments (biomolecule is a protein and therefore the elute contains proteins, col. 36, lines 32-56), wherein each fraction containing an individual protein (individual proteins are present in the fraction and therefore each fraction contains an individual protein; col. 36, lines 32-56) in a sample into a plurality of fractions (col.

35, lines 28-40) and depositing each fraction at a discrete location on a solid substrate to create a plurality of discrete protein enriched locations (col. 35, lines 30-35) for Raman spectra detection (SERS is Raman scattering and produces a Raman spectra, col. 35, lines 30-34), but fail to teach the specific method steps of Raman detection requiring contacting the proteins with a capture probe and contacting a probe/protein complex with a Raman-active probe."

The Office Action further alleges that "Natan et al. (721) teach a method for analyzing the protein content of a biological sample (col. 10, lines 40-47 describe the sandwich assay; col. 10, line 52 describe the target analyte being a protein), comprising: depositing proteins in a separate state at discrete locations on a solid substrate (ligands are attached at specific locations, therefore ligands can be samples in each well which are maintained without cross contamination, col. 25, lines 1-4); contacting the separated proteins deposited at the plurality of discrete protein enriched locations with probes under conditions suitable to form a capture probe/protein complex at one or more discrete locations (col. 3, lines 47-54; col. 10, lines 58-64; at col. 13, lines 45-52 any one of the participants can be immobilized to the substrate surface, a ligand is then bound to the immobilized receptor, protein); contacting the complexes with a Raman-active probe construct that binds to the complex (col. 3, lines 54-63; col. 13, lines 45-52, and Au-conjugated antibody is conjugated with the ligand, which is bound to the immobilized receptor, protein); and detecting Raman spectra produced by the probe construct/protein complexes at the plurality of discrete locations, wherein a Raman spectrum from at a discrete location provides information about the chemical composition of a protein the corresponding discrete protein enriched location by analyzing the protein content of a complex biological sample (col. 23, lines 58-61 discloses SERS detection; Fig. 12 discloses an amplified detection after an unamplified detection; furthermore a change in resonance is detected as the target is brought in contact with the Raman-active probe, therefore the SERS detection occurs before and after contacting the proteins with captured probes and Raman active probes, col. 18, lines 1-5; surface chemical interactions are

analyzed, col. 35, lines 1-5; compounds are identified, col. 24, lines 1-5), in order to provide simultaneous detection of multiple target analytes using a solid support. "

The Office Action finally alleges that "it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the detection of Natan et al. ('264), the Raman detection method steps as taught by Natan et al. ('721), in order to provide increase sensitivity and accuracy of SERS detection."

To establish a prima facie case of obviousness, the following three basic criteria must be met: (1) there must be some suggestion or motivation to modify the reference(s) as proposed by the Examiner; (2) there must be a reasonable expectation of success and (3) the prior art reference(s) must teach or suggest all of the claim limitations.

Applicants have amended claim 38 to include the limitations of claim 27 (not part of this rejection), namely, "analyzing the separated proteins by mass spectroscopy to identify one or more functional groups contained within a separated protein or fragment thereof".

First, Applicants submit that the prior art references fail to teach or suggest all of the claim limitations. Applicants respectfully disagree with the Office Action's allegation that Natan et al. ('264) teaches "chromatographically separating proteins and protein fragments". Natan et al. ('264) teaches a biosensor based on complexes between bimolecule receptors and colloidal Au nanoparticles (Abstract). A review of Natan et al. ('264), particularly col. 36, lines 32-56, does not disclose any teachings of chromatographic separation of proteins and protein fragments. Natan et al. ('721) also does not disclose chromatographic separation of proteins and protein fragments.

In addition, Applicants have amended claim 38 to include the limitations of claim 27 (not part of this rejection), namely, "analyzing the separated proteins by mass spectroscopy to identify one or more functional groups contained within a separated protein or fragment thereof". Accordingly, it is submitted that the cited references, either separately or in combination, fail to teach or suggest all of the claim limitations of amended claim 38.

Second, Applicants submit that there is no suggestion or motivation to modify the references. Natan et al. ('264) teaches a biosensor based on complexes between bimolecule receptors and colloidal Au nanoparticles (Abstract). Natan et al. ('721) teaches methods and reagents for the enhancement of surface plasmon resonance (SPR)- based detection assay (Abstract). There is no suggestion or motivation to modify the biosensor of Natan et al. ('264) with an assay Natan et al. ('721). Accordingly, it is submitted that there is no suggestion or motivation to modify the references.

For at least for the reasons set forth above, it is submitted that the cited references, either separately or in combination, fail to teach or suggest all of the claim limitations, and there is no suggestion or motivation to modify the references. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

B. Claims 2-5, 10, 14-17, 20-26, 29-33 and 38 are rejected under 35 U.S.C. §103(a) as allegedly obvious over Hess et al. (US 6,716,629) in view of Natan et al. (US 6,579,721). This rejection is respectfully traversed.

The Office action alleges that "Hess et al. teach a method comprising: chromatographically separating proteins and protein fragments, wherein each fraction containing an individual protein (sample is prepared using HPLC and liquid eluted from the chromatographic is deposited on a substrate and therefore a plurality of fractions are present, col.

57, lines 5-17; antigen is the analyte and binds to an antibody probe col. 45, lines 53-55, and analyte is in the sample and in the eluate fractions, col. 41, lines 41, lines 8-10) and depositing each fraction at a discrete location on a solid substrate to create a plurality of proteins in a separated state (equi-volume samples are stored on an array and therefore the plurality of proteins are stored in a separated state, col. 57, lines 7-17), wherein detection of the proteins in the eluate is performed of a Raman spectra (col. 41, line 66-col. 42, line 11). Hess et al. fail to teach the specific detection method of detection by Raman spectra."

The Office Action further alleges that Natan et al. (721) teaches the missing elements and "it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the detection of proteins in an eluate of Hess et al,. chromatographic separating compounds into a plurality of fractions, the Raman detection method steps as taught by Hess et al., in order to provide increased sensitivity and accuracy of SERS detection."

Applicants have amended claim 38 to include the limitations of claim 27 (not part of this rejection), namely, "analyzing the separated proteins by mass spectroscopy to identify one or more functional groups contained within a separated protein or fragment thereof". Accordingly, it is submitted that the cited references, either separately or in combination, fail to teach or suggest all of the claim limitations of amended claim 38.

C. Claims 6-9 are rejected under 35 U.S.C. §103(a) as allegedly obvious over Natan et al. (US 6,242,264) in view of Natan et al. (US 6,579,721), as applied to claim 38, further in view of Grow (US 6,040,191). This rejection is respectfully traversed.

As discussed above in part A, Applicants have shown that Natan et al. ('264) and Natan et al. ('721) fail to teach each and every element of amended claim 38, and there is there is no motivation to combine their teachings. Claims 6-9 ultimately depend upon claim 38. Claims 6-9

should be allowable for at least those same reasons discussed above. The addition of Grow does not provide the teachings that are missing from Natan et al. ('264) and Natan et al. ('721) to render the invention obvious, and the combination of them does not disclose or suggest every limitation of claims 6-9. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

D. Claims 11-13 are rejected under 35 U.S.C. §103(a) as allegedly obvious over Natan et al. (US 6,242,264) in view of Natan et al. (US 6,579,721), as applied to claim 38, further in view of Avseenko et al. (Immobilization of Proteins in Immunochemical Microarrays Fabricated by Electrospray Deposition, Analytical Chemistry, 2001, 73, 6047-6052). This rejection is respectfully traversed.

As discussed above in part A, Applicants have shown that Natan et al. ('264) and Natan et al. ('721) fail to teach each and every element of amended claim 38, and there is there is no motivation to combine their teachings. Claims 11-13 ultimately depend upon claim 38. Claims 11-13 should be allowable for at least those same reasons discussed above. The addition of Avseenko et al. does not provide the teachings that are missing from Natan et al. ('264) and Natan et al. ('721) to render the invention obvious, and the combination of them does not disclose or suggest every limitation of claims 11-13. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

E. Claims 18 and 19 are rejected under 35 U.S.C. §103(a) as allegedly obvious over Natan et al. (US 6,242,264) in view of Natan et al. (US 6,579,721), as applied to claim 38, further in view of Storhoff et al. (US 2004/0053222). This rejection is respectfully traversed.

As discussed above in part A, Applicants have shown that Natan et al. ('264) and Natan et al. ('721) fail to teach each and every element of amended claim 38, and there is there is no

motivation to combine their teachings. Claims 18 and 19 ultimately depend upon claim 38 (through claim 17). Claims 18 and 19 should be allowable for at least those same reasons discussed above. The addition of Storhoff et al. does not provide the teachings that are missing from Natan et al. ('264) and Natan et al. ('721) to render the invention obvious, and the combination of them does not disclose or suggest every limitation of claims 18 and 19. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

F. Claims 27 and 28 are rejected under 35 U.S.C. §103(a) as allegedly obvious over Natan et al. (US 6,242,264) in view of Natan et al. (US 6,579,721), as applied to amended claim 38, further in view of Nelson et al. (US 5,955,729). This rejection is moot with regard to canceled claim 27. This rejection is respectfully traversed.

As discussed above in part A, Applicants have amended claim 38 to include the limitations of claim 27, namely, "analyzing the separated proteins by mass spectroscopy to identify one or more functional groups contained within a separated protein or fragment thereof". Applicants have also shown that Natan et al. ('264) and Natan et al. ('721) fail to teach each and every element of amended claim 38, and there is there is no motivation to combine their teachings. Claim 28 ultimately depends upon claim 38. Claim 28 should be allowable for at least those same reasons discussed above. The addition of Nelson et al. does not provide the teachings that are missing from Natan et al. ('264) and Natan et al. ('721) to render the invention obvious, and the combination of them does not disclose or suggest every limitation of claim 28. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

VI. Conclusion

In view of the foregoing amendments and remarks, Applicants submit that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicant's undersigned representative if there are any questions relating to this application.

No fee is believed necessary with the filing of this paper. However, the Commissioner is hereby authorized to charge any fees that are required, or credit any overpayments to Deposit Account No. 07-1896 referencing the above-identified attorney docket number. A copy of the Transmittal Sheet is enclosed.

Respectfully submitted,

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